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Multifaceted intervention to curb in-hospital over-prescription of proton pump inhibitors: a longitudinal multicenter quasi-experimental before-and-after study

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Abstract

Background. Proton pump inhibitors (PPIs) are indicated for a restricted number of clinical conditions, and their misuse can lead to several adverse effects. Despite that, the proportion of overuse is alarmingly high. **Objective.** To test the efficacy of a multifaceted strategy in order to achieve a significant reduction of new PPI prescriptions at discharge in hospitalized patients. **Design**. Multicenter longitudinal quasi-experimental before-and-after study conducted from July 1^{st}2014 to June 30^{th}2017.**Participants**.44,973 admissions in a network of 5 public teaching hospitals of the Italian-speaking region of Switzerland. **Intervention.** Multifaceted strategy consisting in a continuous transparent monitoring-benchmarking and in capillary educational interventions applied in the internal medicine departments. To confirm the causality of the results we monitored the trend of new PPI prescriptions in the, not exposed to the intervention, surgery departments of the same hospital network. **Main Measures.** New PPI prescriptions at hospital discharge. **Key results.** Over the 36 month study period 44,973 patient files were analyzed. At admission, comparing internal medicine vs. surgery departments, 44.9% vs. 23.3% of patients were already being treated with a PPI. The annual rate of new PPI prescriptions, for internal medicine showed a decreasing trend: 19, 19, 18, 16% in years 2014, 2015, 2016, 2017, respectively ($p<0.001$, 2014 vs. 2017; p-for-trend<0.001), while an increasing rate was found in the surgery departments in the same years: 30, 29, 36, 36%, respectively ($p<0.001$, 2014 vs. 2017; p-for-trend<0.001). The case mix was significantly associated with the probability of new PPI prescriptions in both departments (OR1.35, 95% CI 1.26-1.44 for internal medicine and 1.24, 95% CI 1.19-1.30 for surgery). **Conclusions.** The introduction of a multifaceted intervention significantly reduced the time trend of PPI prescriptions at hospital discharge in internal medicine departments. Further studies are needed to confirm whether the strategy proposed could contribute to optimize the in-hospital drug prescription behavior in other healthcare settings as well.

Keywords

Choosing Wisely

Proton Pump Inhibitors

Overprescribing

Physician empowerment

Transparent prescription monitoring

Prescription benchmarking

Abbreviations: Proton Pump Inhibitors (PPIs), Case Mix (CM)

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Background.

Over and inappropriate use of proton pump inhibitors (PPIs) represent a global healthcare problem leading to significant adverse effects and economic consequences worldwide [1,2]. Despite the fact that the use of PPIs should be limited to a well-defined spectrum of clinical conditions [3], the rate of new prescriptions in in- and outpatients is still very high, reaching a percentage of inappropriateness of more than 50% in patients being admitted to hospitals [4,5]. These data are even more alarming considering that the prescription of PPIs, as stated above, is linked to several potential adverse effects such as infections (Clostridium difficile, colitis) [6], bone fractures (hip and spine) [7], hypomagnesaemia and related electrolyte disturbances [8], nutritional deficiencies [9], acute and chronic kidney diseases [10,11] and possibly, ischemic heart disease [12], dementia [13] and gastric carcinoids [14].

Many factors could influence the sustained inappropriate use of PPIs, among which the sometimes uncritical continuation of primary care physicians' medications during the hospital stay, as well as the chronic renewal of PPI prescriptions after patients' discharge from the hospitals [15-17].

In hospitalized patients the initiation of a therapy with PPIs should be limited to specific clinical conditions, such as gastritis, gastro-esophageal reflux diseases, gastrointestinal bleeding and stress and medication related gastric ulcer prophylaxis [18]. Overuse is however frequent in this setting and mainly related to disregard of recommendations and to liberal interpretations of indication in the prevention of stress ulcers with potential adverse drug events in a context of minimal expected benefit on clinical outcome [18].

Several efforts targeted at reducing PPI prescriptions in hospitalized patients have been described; e.g. promoting the use of the minimum effective dose and affording different diagnoses or treatments in unresponsive patients to PPIs therapy [19]. At the international level the "Choosing Wisely" campaign advises physicians not to prescribe medications for stress ulcer prophylaxis to medical inpatients unless at high risk for complications [20].

Nevertheless, interventions targeting PPI prescriptions still represent an important public health challenge, mostly at the hospital level where the rate of potentially inappropriate prescriptions sometimes reaches dramatic levels [21].

To date, no multifaceted interventions targeted to decrease PPI prescriptions have been evaluated in the hospital setting.

We proposed therefore a strategy based on a multi-level decision-making intervention: 1) educational intervention, based on the concept of patient-centred medicine [22], aimed to raise awareness about PPIs overtreatment, prescription inappropriateness and side effects; and 2) a continuous transparent monitoring system enabling in-hospital healthcare providers to open benchmarking and to optimize new PPI prescriptions in a proactive and comprehensive approach.

Our hypothesis was that a continuous transparent monitoring system combined with an educational intervention would lead to a significant reduction of new PPI prescriptions at discharge.

The primary study objective was hence to obtain a significant decrease in the rate of new PPI prescriptions in the internal medicine departments following the implementation of the intervention. Secondary study objectives were i) to verify the absence of new prescription reduction in surgery departments, where the staff was also exposed to the publication of internal and targeted Choosing Wisely recommendations but in the absence of involvement in the open benchmarking and in the active educational intervention (controls) ii) to identify factors independently associated with new PPI prescriptions.

Materials and Methods

We conducted a multicenter longitudinal quasi-experimental before and after study from July 1st 2014 to June 30th 2017 in a network of 5 teaching public hospitals (Ente Ospedaliero Cantonale, EOC) of the Italian-speaking part of Switzerland (Flow-Diagram of the Study, **Appendix 1**). We considered in the analysis data of all inpatients admitted in the internal medicine departments (intervention group) during the study period, and compared them to all inpatients admitted in the surgery departments (control group). The hospitals involved in the study were 5: H1, H2, H3, H4 and H5 and all were organized in internal medicine and surgery departments. The internal medicine and the surgery departments included respectively the following units: general internal medicine, geriatrics, nephrology and general surgery, orthopedic and traumatology, and vascular and thoracic surgery.

Basic demographic data and information on diagnoses and case mix (CM) were collected from the electronic patient records of the hospitals. The CM, as relative value assigned to the patients' Swiss Diagnosis-Related Group at hospital discharge, is an indicator of illness severity used to calculate hospitals' reimbursements [23].

The study was compliant with the "Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement" guidelines [24]. According to Swiss law, studies based solely on anonymous secondary data do not require approval from an ethics review board [25].

The multifaceted intervention was implemented stepwise over the 36 month study period (**Figure 1**) and was aimed at improving hospitals' PPI prescriptions by: i) educational interventions based on implementation of hospitals' best-practice guidelines (see **Appendix 2** for internal recommendations), promoting awareness of the potential prescription inappropriateness and side effects of PPIs; and ii) continuous transparent monitoring/benchmarking of new PPI prescriptions.

The intervention was applied in the internal medicine departments, while the data of the surgery departments were used as controls to further evaluate the impact of the strategy. The educational intervention included face-to-face feedbacks and meetings and educational outreach visits by local opinion leaders. Healthcare providers were sensitized at different levels on the importance of i) making wise decisions in PPI prescription (sharing with patients information on risks about the medication and on evidence of over- and inappropriate prescriptions); ii) identifying patients in which PPIs are not indicated and/or are potentially dangerous; iii) withdrawing PPIs when not, or no longer indicated iv) promoting behavior changes by consulting the monitoring/benchmarking platform on new PPI prescriptions. The educational intervention was based on multiple components making it a ‘complex educational intervention’ in which the full spectrum was targeted to change physicians' behavior.

A. **Educational meetings**: educational meetings were held repeatedly and capillary in the department of the intervention. In each meeting feedback and management guidelines on PPI prescriptions were discussed with all healthcare providers involved. The educational meetings were conducted by a group of experts composed of at least 2 clinicians (a specialist in general internal medicine and a specialist in medical pharmacology), a biostatistician and an expert in quality and patient safety.
B. **Educational materials**: printed and electronic versions of the internal guidelines, as rapid clinical-decision making supports, were distributed in a capillary way; pocket-forms were also available (see Appendix 1). The recommendations were based on national and international guidelines.
C. **Electronic media communication**: healthcare providers of all services of the intervention group received email newsletters periodically with key educational messages.

The continuous transparent monitoring/benchmarking of new PPI prescriptions consisted in a centralized, transparent platform (i.e. allowing unrestricted access to data by all health care providers involved in the project), called “Reporting Wisely”, able to collect weekly updated data about new PPI prescriptions, and to perform variability analysis and benchmarking both internally, according to time, for the same hospital by units, services and departments and externally at the network level. User friendly continuously updated graphics depicting the results of the monitoring were also available for any evaluation by the physicians and nurses of the staff involved in the project of the internal medicine departments.

The primary outcome of the study was to obtain a significant reduction in the rate of new PPI prescriptions at hospital discharge. New PPI prescriptions were considered as the presence in the medication list, given to the patient at hospital discharge, of at least one drug belonging to the PPI class in a previously naïve patient.

Statistical analysis

A relative reduction of new PPI prescriptions of 15% was considered as relevant. It was calculated that a sample size of 4142 patients was required to test the hypothesis that the intervention was efficient in producing a decrease of PPI prescriptions from 20 to 17% (relative reduction of 15%). Calculations used a one sided significance of 0.05 and a power of 80%. Power calculations were carried out using G*Power (V.3.1.7).

Baseline characteristics were summarized using the median and the interquartile range or frequencies and percentages, as appropriate. Data were analysed into two groups based on the hospital department (internal medicine vs. surgery; i.e. intervention vs. non-intervention). Comparisons were performed using an independent samples *t*-test or a Chi-square test, as appropriate. Temporal trends of new PPI prescriptions were examined and analyzed by calendar quarter, considering the two departments separately. Quarterly and annual rates of new PPI prescriptions were calculated and differences were evaluated using the Chi-square test. Changes over time in the percentage of new PPI prescriptions were examined using Chi-square tests for trends.

A multivariate regression analysis was performed to identify factors independently associated with new PPI prescriptions (dependent variable). Fully adjusted models included fixed effects for years (2014, 2015, 2016, and 2017), hospitals (H1, H2, H3, H4, and H5), hospital-year interaction, gender, age, and the individual Case Mix. Odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. R statistical software (www.r-project.org) was used for data analysis. Statistical significance for all outcomes was set at $p \leq 0.05$.

Results

Overall, 44,973 patient files over the 36 months of the monitoring and intervention period were analyzed. **Table 1** summarizes the characteristics of the study population in the internal medicine and surgery departments. The median age of the study participants was 75 years for internal medicine (intervention group) and 67 years for surgery (control group). Most patients were older than 65 years in both departments and the Case Mix (CM) was slightly higher in the surgery departments (0.80 vs 0.70). At admission, 44.9% of the patients were already taking PPIs in internal medicine vs. 23.1% in the surgery departments. The proportion of patients already treated at the admission with a PPI among age groups (<65; 65-80 and >80 years) was 31.8, 49.9 and 50.3% in the internal medicine: and 12.9, 30.2 and 36.7%. in surgery. At discharge, new PPI prescriptions in internal medicine and surgery departments were 18.1 and 32.8%, respectively. New PPI prescriptions among age groups (<65; 65-80 and >80 years) for internal medicine and surgery departments were 38.4, 36.9 and 24.7% and 53.7, 31.4 and 14.9%, respectively. Admissions for, and diagnosis of upper gastrointestinal bleeding during the hospital stay, did not increase significantly during the observation (2.0, 1.9, 2.1 and 2.1% in 2014, 2015, 2016 and 2017 respectively). The time trend of new PPI prescriptions at discharge for each hospital of the network by departments showing an important inter- and intra-institutional variability is represented in **Figure 1** and **Figure 2**. For the internal medicine department the crude rate of new PPI prescriptions decreased over the study period, from 18 (year 2014) to 16% (year 2017) (p <0.001); (**Figure 1**). The annual rate, for the department of internal medicine, also shows a decreasing trend: 19, 19, 18, and 16% in 2014, 2015, 2016, and 2017, respectively (p for trend <0.001) (**Figure 2**). For the surgery departments, where the intervention was not applied, an increasing yearly trend in new PPIs prescriptions was on the contrary found: 30, 29, 36 and 36% in 2014, 2015, 2016 and 2017, respectively (p<0.001, p for trend <0.001); year 2014 vs. year 2017: 30 vs. 36% (p<0.001).

In **Figure 3** the trends by quarter of new PPIs prescription across the hospital network, by department, are shown.

In **Figure 4** we investigated whether the rate of new PPI prescriptions varied among the different age groups over the study period in both departments under analysis. In the internal medicine department for the age group < 65 in the years: 2014, 2015, 2016, 2017 the rate of new PPI prescriptions were: 22.4, 21.7, 19.1 and 18.5 %, respectively (p for trend 0.015). The difference in the rate of new PPI prescriptions in the same age group before vs. after the intervention (years 2014-2015 vs. 2016-2017) was significant (p 0.013) (**Figure 4A**). Differences in temporal trends among the other age groups were on the contrary non-significant. In the department of surgery, in the age group <65 we detected a significant increase in the rate of new PPI prescriptions: 31.7, 30.0, 36.1 and 41.0% in the years 2014, 2015, 2016 and 2017, respectively (p for trend <0.001) (**Figure 4B**). An increasing temporal trend was also found for the age groups 65-80 and >80 years (p<0.001 for both).

We used logistic regression to model the probability of receiving a new PPI prescription during hospitalization, by department (**Table 2**). For the internal medicine department the odds ratio of having a new PPI prescription decreased significantly with age (OR= 0.99; 95% CI 0.99-1.00; p<0.001) and increased with CM (OR =1.33; 95% CI, 1.24-1.43, p<0.001). Gender on the contrary did not appear to affect the probability of a new PPI prescription. Compared with 2014 (when the monitoring started), the odds of new PPI prescriptions was significantly lower in 2017 (the third year of the intervention), with an odds ratio of 0.82 (95% CI, 0.71-0.96; p=0.014). For the department of surgery the multivariate analysis revealed that the probability of receiving a new PPI prescription was lower for males (OR = 0.86; 95% CI 0.80-0.92; p<0.001) and increased with CM (OR 1.24, 95% CI 1.19-1.30; p<0.001.), and over time (for the year 2017 compared with 2014, OR = 1.29, 95% CI, 1.14-1.47, p<0.001).

4. Discussion

We designed and implemented a multifaceted multilevel intervention and evaluated its effectiveness in curbing the prescription of proton pump inhibitors in hospitalized patients at discharge.

Our intervention resulted in statistically significant reduction over time in PPI prescriptions in the internal medicine departments (p for trend 0.02), where the program was applied. Its effectiveness was further confirmed analysing the opposite temporal trend of new PPI prescriptions in the surgery departments (p for trend <0.001) where targeted actions on the contrary were not applied and where the prescription behaviour over time suggests an "epidemic pattern" of continuous growth. The magnitude of the relative reduction in PPI prescriptions in the intervention department of about 16% (absolute reduction 3%) is not numerically impressive but consistent if the 3 year follow-up is considered. Reducing inappropriate PPI prescriptions in the hospital setting represents an important public health challenge and is a topic of continuous targeted interventions; as in our case however (the surgery department was exposed to the specific Choosing Wisely and internal recommendations but not to the capillary educational program and to the prescription monitoring/benchmarking), only the use of multifaceted interventions, have until now shown consistent and sustained results in influencing medication prescription strategies and poly-pharmacy [26,27]. The aim of the study was to analyze and optimize PPI prescriptions at discharge in previously untreated patients. The rationale was to stop the epidemic long-term PPI prescription wave, by concentrating on one of the key actors of the process; that is to say the hospital care givers. The prescriptions limited to the in-hospital stay were however not analyzed. Previous studies aimed at ameliorating PPI prescriptions in the hospital setting have been published [28]; the efficacy of multifaceted intervention in this setting was, however, not convincingly demonstrated. Embracing the principles of the "Choosing Wisely" philosophy based on high value care and shared decision making, we targeted a higher level of awareness and "positive" and "negative" guideline compliance in the prescription behaviors. Findings from our study indicate that a multilevel strategy (transparent monitoring-benchmarking system associated with capillary educational interventions) could be a useful way to face the issue of the inadequacy of new PPI prescriptions in hospitalized patients. Negative consequences of the restrictive PPI prescription policy were not seen; admissions for, and diagnosis of upper gastrointestinal bleeding during the hospital stay, did not increase significantly (2.0, 1.9, 2.1 and 2.1% in 2014, 2015, 2016 and 2017 respectively). Our intervention could have been effective due to four key elements: transparent benchmarking, knowledge sharing, reflective practice, and supportive-interactive tools. We believe that the intervention here proposed on top of the usual strategy based on dispensing recommendations and "positive" and "negative" guidelines, significantly contributed to reducing PPI prescriptions, by progressively generating an attitudinal change. The possibility of continuously monitoring their own prescriptive behavior and comparing it to that of the other institutions involved, could definitely represent a strong stimulus encouraging clinicians to undertake immediate actions. As shown in previous studies [29], we also demonstrated that the educational outreach based on training healthcare providers to supply high-value care supported by sensitive data is more effective in generating prescription awareness and adaptive behavior than passive guideline dissemination. Overall the strengths of our intervention can be summarized in several key points: i) multifaceted structure in the hospital setting (most of the previous multifaceted studies on PPI prescription were conducted at the primary care level [30,31]); ii) the intervention was carried out over a long period of time (36 months); one of the longest observation periods in this field [30,32]; iii) the efficacy of the intervention was assessed on a large multicenter population, in a network of internal medicine departments; iv) the educational intervention was based on multiple components and unlike other studies several educational meetings were held [33,34]; v) most of the previous studies had de-prescription of PPI as the primary outcome; while our primary outcome was to contain new prescriptions [35-37]; vi) in our study we involved, with motivational letters, general practitioners in the campaign, hoping to curb the vicious circle of inappropriate prescriptions.

We also showed that the Case Mix was significantly associated with the risk of having a new PPI prescription in both departments under analysis (OR 1.33; 95% CI 1.24-1.43 internal medicine department; OR 1.25, 95% CI 1.19-1.31, surgery department). This could be of interest because recently an association between cardiac and metabolic diseases, both significantly impacting the CM, and the over-prescription of PPIs was documented [38]. Surprisingly, in our study, in the internal medicine department, age seemed to reduce the probability of receiving new PPI prescriptions (OR 0.99; CI 0.99 - 1.00), which is apparently in contrast with our internal recommendations, in which age > 65 years is highlighted as one of the risk factors to be considered as a trigger for PPI prescription. We believe that this finding could have been related to peculiar interconnected and potentially confounding aspects of the study population, mainly related to the spectrum of diseases, potentially justifying new or former PPI prescriptions [31-34], and the percentage of PPI untreated patients at hospital admission (50% versus 32% in over and under 65 years respectively in our study), which both vary significantly between age groups. Our study has however some limitations that should be acknowledged. The first one is related to the quasi-experimental design; randomized controlled trials should indeed be used to evaluate the effectiveness of interventions. Furthermore, in relation to the study design, we have to acknowledge that the intervention group and the surgery departments used as an indirect "control", differed in the characteristics of both patients and providers. The prescription behavior of the surgery departments was analyzed to either reinforce or weaken the hypothesis that the improvement targeted in the internal medicine department would have been a consequence of the intervention. Comparison between groups should be read in the perspective of the global PPI prescription temporal trend. We can therefore not definitively prove causation between the implementation of our strategy and the outcome. Moreover, we did not assess whether or not the reduction in new PPI prescriptions obtained in the departments of internal medicine improved appropriateness and/or translated into a better clinical outcome and finally we cannot be sure that the observed reduction in new PPI prescriptions will persist over time. The intervention was addressed to clinicians and healthcare providers working in a network of teaching hospitals, therefore diversified in terms of age, years of practice, and overall with different personal sensibility towards the Choosing Wisely Campaign. Thus caution is needed in generalizing the findings to other clinical settings and to other populations.

Further studies are needed to confirm the results and to explore the impact on clinical outcome.

Conclusions

Over-prescription of PPIs at the hospital level is a big concern worldwide. The initial benchmarking at the network level helped us to understand that recommendations and guidelines alone, repeatedly proposed in the recent years, would not lead to behaviour changes. Appropriate prescriptions call for deliberate judicious treatment strategies based on knowledge of the evidence/guidelines (education), awareness of the roots of one's own prescription behaviour (transparent monitoring and benchmarking), motivation (transparent monitoring and benchmarking), and is reinforced by encouraging conversations between patients and clinicians on the risks of unnecessary care (education). Embracing the philosophy of Choosing Wisely we have built a multifaceted and multilevel improvement strategy, supported by supportive-interactive tools helping clinicians to build awareness and to change habits. Given the positive findings presented here, we plan to further model the intervention components to reinforce even more the physician and patient compliance.

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Availability of data and materials

The datasets from the current study are not publicly available but are available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

All authors have provided consent to publish.

Ethics approval and consent to participate The study is exempt from institutional review board approval of the Swiss Ethics Committee because it involved anonymous secondary data only. http://www.kofam.ch/it/domanda-e-procedura/progetti-non-soggetti-allobbligo-di-autorizzazione/.

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Tables and figure Legends

Table 1. Characteristics of the study population (44,973 admissions) by departments for the study period 2014-2017.

	Internal Medicine Department	**Surgery Department**
Admissions (n.)	26.312	18.661
H1, n (%)	2.995 (11.4)	1.536 (8.2)
H2, n (%)	4.975 (18.9)	3.273 (17.5)
H3, n (%)	6.558 (24.9)	4.545 (24.4)
H4, n (%)	5.805 (22.1)	4.531(24.3)
H5, n (%)	5.976 (22.7)	4.776 (25.6)
Age, years (median, Q1-Q3)	75 (63-83)	67 (50-78)
Age groups, n (%)		
<65, y	7.200 (27.4)	8.658 (46.4)
65-80, y	10.107 (38.4)	6.241 (33.4)
>80, y	9.005 (34.2)	3.762 (20.2)
Gender, females (%)	13.129 (49.9)	9.630 (51.6)
Case-mix (median, Q1-Q3)	0.70 (0.51-0.92)	0.80 (0.53 -1.49)
PPIs admission, n (%)	11.829 (44.9)	4.339 (23.3)
PPIs discharge, n (%)	13.337 (50.7)	8.534 (45.7)
New PPI prescriptions, n (%)	2.617 (18.1)	4.696 (32.8)
New PPI prescriptions by hospital		
H1, (%)	328 (12.5)	546 (11.6)
H2, (%)	379 (14.5)	487 (10.4)
H3, (%)	747 (28.5)	1.316 (28.1)
H4, (%)	481 (18.4)	772 (16.4)
H5, (%)	682 (26.1)	1.575 (33.5)
New PPI prescriptions by age groups, n (%)		
<65, y	1.004 (38.4)	2.524 (53.7)
65-80, y	967 (36.9)	1.472 (31.4)
>80, y	646 (24.7)	700(14.9)

Table 2. Multivariate analysis of factors associated with receiving a new PPI prescription at hospital discharge, by department.

	Internal Medicine Department	
	OR (95% CI)	**p-value**
Hospitals		
H1	1 [Reference]	
H2	0.56 (0.47 - 0.66)	<0.001
H3	0.91 (0.78 -1.05)	0.199
H4	0.57 (0.48 - 0.66)	<0.001
H5	0. 92 (0.79 - 1.07)	0.254
Year of the study		
2014	1 [Reference]	
2015	1.01 (0.89 - 1.14)	0.918
2016	0.92 (0.81 - 1.05)	0.220
2017	0.82 (0.71 - 0.96)	0.014
Gender		
Female	1 [Reference]	
Male	0.99 (0.90 - 1.08)	0.783
Age	0.99 (0.99 - 1.00)	<0.001
Case Mix	1.35 (1.26 -1.44)	<0.001
	Department of Surgery	
Hospitals		
H1	1 [Reference]	
H2	1.02 (0.77-1.35)	0.899
H3	1.39 (1.07-1.79)	0.013
H4	0.69 (0.52-0.91)	0.010
H5	1.20 (0.92-1.56)	0.176
Year of the study		
2014	1 [Reference]	
2015	0.95 (0.85 -1.06)	0.327
2016	1.30 (1.17 - 1.45)	<0.001
2017	1.29 (1.14 - 1.47)	<0.001
Gender		
Female	1 [Reference]	
Male	0.86 (0.80 - 0.92)	<0.001
Age	1.0 (1.0-1.01)	0.696
Case Mix	1.24 (1.19-1.30)	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval.

Figures Titles and Legends

Figure 1:

Title:

Rate time trends of new PPI prescriptions in the internal medicine departments where the intervention took place.

Legend:

Rate of new PPI prescriptions in the internal medicine departments, calculated quarterly. Dashed lines represent 95% pointwise confidence intervals. A decreasing temporal trend in PPI prescriptions over the study period was found (p for trend <0.001). The temporal pattern of the interventions is depicted in the upper part of the figure.

Figure 2:

Title:

Rate time trends of new PPI prescriptions in the surgery departments, where there was no intervention.

Legend:

Rate of new PPI prescriptions in the surgery departments, calculated quarterly. Dashed lines represent 95% pointwise confidence intervals. An increasing temporal trend in PPI prescriptions over the study period was found (p for trend <0.001).

Figure 3

Title:

Trends by quarter of new PPI prescriptions throughout the hospital network, by department.

Legend:

Intra- and inter-hospital variability of new PPI prescriptions during the study period by departments. The rate over time is represented for each quarter of the study years.

Figure 4

Title:

Rate of new PPI prescriptions within age groups over the study period.

Legend:

Panel A. Internal medicine departments: a significant decrease in the rate of new PPI prescriptions in the age group < 65 years during the study period was found (p for trend 0.015). **Panel B**. Surgery departments: a significant increase in the rate of new PPI prescriptions in all age groups over the study period was found (p for trend <0.001).